

ABSTRACT

The present invention relates to compositions and methods for reducing cholesterolemia and its effects. More specifically, the invention is directed, in one embodiment, to methods for screening for compounds that affect cholesterol levels generally, and in particular, that affect the absorption of cholesterol. The invention also is directed to methods of screening for compounds that increase bile acid synthesis. In so doing, the inventors describe useful transgenic cells and animals which lack one or both alleles of the LXR α gene. Also provided are therapeutic methods designed to reduce cholesterol levels in suitable subjects. The reduction may be effected by decreasing cholesterol absorption, increasing bile acid synthesis, or combinations thereof. Particularly useful in decreasing cholesterol absorption are RXR agonists, for example, rexinoid compounds. Therapeutic intervention in cholesterol biosynthesis and diet are additional adjunct therapies. In addition, the present invention relates to candidate compounds that modulate the expression of ABC-1 in a cell that expresses RXR. Methods of identifying and making a modulator of ABC-1 are disclosed.